induces ectopic hair follicle formation and this process is dependent on the activation of several downstream pathways, including Hedgehog, Notch and vitamin D receptor signalling. Hedgehog provides a proliferative stimulus, while Notch and vitamin D promote differentiation. Perturbation of Wnt signalling contributes to the development of keratinocyte tumours in mice and humans.

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Program/Abstract # 48
Fam20b and Xylosyltransferase1 (Xylt1) drive cartilage matrix production and inhibit perichondral bone during endochondral ossification

Brian F. Eames, Mary E. Swartz, Charles B. Kimmel
Institute of Neuroscience, University of Oregon, Eugene, OR, USA

To gain insight into tissue interactions between developing cartilage and overlying perichondrium that regulate endochondral ossification, we used forward genetics to identify three zebrafish mutants with decreased Alcian blue staining of cartilage along with premature and, later, increased Alizarin red staining in the perichondrium. Genetic mapping and subsequent genomic sequencing revealed mutations at two loci. *b1128* contained a splice site mutation in *xylt1*, which encodes a proteoglycan enzyme, producing frameshifted transcripts. *b1125* and *b1127* exhibited early stop and missense mutations, respectively, in *fam20b*, a recently identified gene of unknown function. Splice-site morpholinos against *fam20b* phenocopy both cartilage and bone features of mutants. Double mutant analyses indicate that *fam20b* and *xylt1* operate in a linear pathway for proteoglycan production; analyzing *fam20b* expression in *xylt1* mutants and vice versa will reveal a relative pathway order. In wild-type embryos, *fam20b* and *xylt1* appear to be expressed in cartilage, but not in perichondrium, suggesting that the mutant perichondral bone phenotype results from an indirect influence of cartilage on overlying perichondral osteoprogenitors, a hypothesis we are testing with mosaic analysis. As cartilage cells mature, they decrease Alcian blue staining, a feature characteristic of our mutants, and they also up-regulate osteoinductive factors, the signaling of which is known to be affected by proteoglycans. Therefore, we are testing whether loss of the Xylt1/Fam20b pathway promotes premature cartilage cell maturation.

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Program/Abstract # 49
Pluripotency and the onset of differentiation in the *C. elegans* soma

Susan E. Mango, Tanya Yuzyuk, Tala Fakhouri
Department of Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA

The transition from naive precursor towards the differentiated state is characterized by sequential waves of gene expression that are governed by regulatory transcription factors. The goal of our research is to understand how transcriptional circuitry dictates the progression from pluripotency, to cell-fate specification and ultimately differentiation. We have defined a window in early embryogenesis when cells are developmentally plastic, while after this stage cells are restricted in their cell-fate potential. We have used a range of molecular and cell biological approaches to characterize the pluripotent state, and to define the changes that accompany the loss of pluripotency and differentiation onset. These cellular behaviors reveal large-scale reorganization of the nucleus at the onset of differentiation. To begin to define the molecular mechanisms that underlie these changes, we have examined regulators of histone modifications involved in transcriptional silencing. The data implicate these regulators for the loss of pluripotency and the acquisition of cell fate.

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Program/Abstract # 50
APC inhibits supernumerary tooth formation during embryogenesis and throughout adulthood

Xiuping Wang, Danniel O'Connell, Jennifer J. Lund, Irfan Saadi, Mari Kuraguchi, Annick Turbe-Doan, Raju Kucherlapati, Richard L. Maas
Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, MA, USA

Mouse incisors grow continuously throughout life and contain stem cells at the apical end of the cervical loop region. Adenomatous polyposis coli (Apc) is an inhibitor of canonical Wnt signaling pathway. Apc, together with Axin and GSK3, bind to β-catenin, and send it for degradation. To understand the role of Apc in the regulation of dental stem cells, we deleted Apc gene in the epithelium under Keratin 14 promoter. This results in the formation of numerous supernumerary teeth at multiple regions within the jaw. The formation of supernumerary teeth is Apc cell-autonomous. Only a small number of Apc deficient cells are able to recruit the surrounding wild type epithelial cells and induce the adjacent mesenchymal cells into a new odontogenic program. Increased canonical Wnt signaling upregulated Pitx2, Fgf8, and Fgf4, which are all critical genes for new tooth germ initiation. In addition, the timing for the formation of supernumerary teeth is compressed compared to the endogenous teeth. By using tamoxifen inducible conditional mice to knockout Apc or constitutively activate β-catenin in adult mouse epithelium, we showed that the adult mice still have the potential to form new teeth, indicating that Apc inhibits supernumerary tooth formation during embryogenesis and throughout adulthood. These results shed light on the therapeutic potential of regenerating new teeth and may also give hints to the tissue engineering of other organs.

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